DOCKET NO: 267336US0PCT

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF	:
HANS-ULRICH PETEREIT, ET AL.	: EXAMINER: WESTERBERG
SERIAL NO: 10/532,831	:
FILED: MARCH 9, 2006	: GROUP ART UNIT: 1618
FOR: MULTILAYER DOSAGE FORMS, WHICH CONTAIN ACTIVE SUBSTANCES AND WHICH COMPRISE A NEUTRAL CORE, AND AN INNER AND OUTER COATING CONSISTING OF METHACRYLATE COPOLYMERS AND METHACRYLATE MONOMERS	:

REPLY BRIEF

COMMISSIONER FOR PATENTS
ALEXANDRIA, VIRGINIA 22313

SIR:

This Brief is submitted in response to the Examiner's Answer (hereinafter "Answer") of July 20, 2010 pursuant to 37 C.F.R. 41.41.

Applicants do not contest that the polymers used in the claimed multilayer were known. The issue in this appeal, in addition to the arguments made in Appellant's Appeal Brief, is whether one of ordinary skill in the art at the time of invention would have had a reasonable expectation that the claimed form would exhibit:

the values for the percentage release of active substance in a hypotonic and an isotonic release medium based on phosphate buffer pH 6.8 do not differ from one another at any time in the period from 1 to 5 hours by more than 10% (See Claim 1) when the active substance is provided in the inner methacrylate coating (see Claim 1 part b)).

Appellants submit that this would not have been reasonably expected while the Examiner takes the view that this would have naturally flowed from the prior art and/or is not unexpected (see, e.g., pages 9-11 of the Answer).

Appellants position is back by experimental factual evidence, whereas the Examiner's position is based on conjecture, inapplicable law, and a failure to understand the role of rebuttal evidence in the analysis of obviousness rejections.

The facts that back up the Appellants position.

(1) The claims define the specified arrangement, see:

the active substance is provided in the inner methacrylate coating (see Claim 1 part b))

(2) The claims define the unexpected result, see:

the values for the percentage release of active substance in a hypotonic and an isotonic release medium based on phosphate buffer pH 6.8 do not differ from one another at any time in the period from 1 to 5 hours by more than 10% (See Claim 1).

(3) The Examples of the present application demonstrated that when a pharmaceutically active substance is bound to the methacrylate polymer of the inner coat (as defined in Claim 1), the release was not affected by the ionic coat (which is also defined as a limitation in Claim 1). These results show that the release of the active from the pellet is unaffected by the osmotic conditions in the release medium. Again, referencing Example 1 and FIG. 2 above, the conclusion that is drawn from these experiments is that the inner methacrylate polymer, e.g., Eudragit® NE30D was responsible for this unexpected effect. Notably, Example 6 uses a different inner copolymer, i.e., Eudragit® Rl 30D (not within the defined parameters in the claims) and as shown in FIG. 6 the replacement of Eudragit® NE30D with Eudragit® RL30D as the inner coat to which the active is bound had differential release depending on the osmotic conditions of the release medium. Thus, Appellants have

provided evidence demonstrating that their selection of the inner methacrylate polymer, e.g., Eudragit® NE30D compared to other known coating polymers as taught by the cumulative citations was responsible for this unexpected effect.

The art cited in the rejections do not teach the selection and arrangement of polymers with the active substance as claimed and certainly do not provide a reasonable expectation for the release criteria defined in the claims.

On pages 9-10 of the Answer, the Examiner finds that the claimed invention is merely claiming a new property of an otherwise known material citing *Atlas Powder Co. v Ireco, Inc.*, *In re Best*, and MPEP 2112 (citations omitted). These citations primarily deal with facts pertaining to inherent anticipation and even though inherency may be germane in an obviousness analysis (see MPEP 2112), the cited prior art here does not describe the arrangement of the active with the selection of the polymer as claimed.

On page 10 of the Answer, the Examiner newly cites a publication of Knop (*Eur J Pharm Sci* 1996) for the proposition that "release of theophylline from 'neutral PPMA' coated dosage forms (EUDRAGIT®NE30D was the 'neutral PMMA' material) was independent of the pH and buffer solution composition (Section 2.1 ¶4; Section 2.3.1; Section 3.2.5). First, Knop teaches coating a core, the core containing an active (see section 2.3.1) and the relevant behavior of that arrangement of coating and active is not directly applicable to the arrangement as claimed where again the active is contained in the coating itself (see Claim 1, part b)) nor has the Examiner suitably explained why this different arrangement is applicable. See In re Sullivan, 84 USPQ2d 1034 (Fed. Cir. 2007) "the PTO bears the initial burden of presenting a prima facie case of unpatentability..." Further, while Knop assessed the release in different buffers, namely formate buffer, citrate buffer, and phosphate buffer (see FIG. 4 and Section 2.2), the Examiner makes no attempt to explain or provide any evidence, thereby failing to satisfy the required burden required, that these buffers are

differentially hypotonic and/or isotonic to yield any suitable information germane to the limitation in Claim 1: "***the values for the percentage release of active substance in a hypotonic and an isotonic release medium based on phosphate buffer pH 6.8 do not differ from one another at any time in the period from 1 to 5 hours by more than 10%.***"

Further, the Office continues to misapprehend the evidentiary effect of unexpected results. In it's understanding, if it believes that it has made a *prima facie* case, no results provided by the invention could possibly be unexpected because they flow naturally from following the suggestion of the prior art. In essence, the Office fails to understand the role of rebuttal evidence. The Examiner provides her own view of what would have been proper rebuttal evidence in the discussion bridging pages 11-12 of the Answer where two layers were applied. However, this submission makes it abundantly clear that the Examiner is not properly considering the actual evidence of record. That is, as explained in detail in Appellant's Appeal Brief, the inner coating layer, e.g. Eudragit®NE30D was responsible for the effect that is deemed to be not reasonably expected by the inventors.

Appellants must emphasize again that it is legal error for the Office to dismiss a showing of unexpected results as flowing from or inherent in the Examiner's prior art construct (in this case, the combination of Ulmius and Beckert or Gang). See again, *In re Sullivan, Id.*

Rather than considering Appellants showing of unexpected results as rebuttal evidence to an alleged *prima facie* case, the Examiner has dismissed it and, in fact, has clearly convinced herself (and apparently two SPEs) that unexpected results cannot exist when she thinks she has made a *prima facie* case. This is clear legal error.

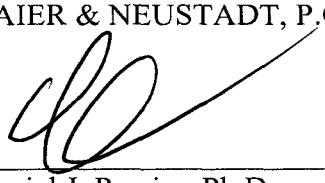
In addition to their showing that there is no *prima facie* case, Applicants have shown an unexpected improvement in resistance to the osmolarity of the dissolution medium into which the claimed form is placed. The Examiner has put forth insufficient reasoning that

would support a conclusion that, *looking forward*, such an improvement would have been expected from the combination of Ulmius and Beckert or Gang. Rather, the Examiner looks backwards and concludes that because it is her opinion that the references present a *prima facie* case any property, benefit, or characteristic of the invention Applicant wishes to discuss in rebuttal is meaningless. As the Board is aware, this is completely improper and, at best, is a classic case of requiring comparison of the results of the invention with the results of the invention. See MPEP 716.02(e) and *In re Chapman*, 357 F.2d 418, 148 USPQ 711 (CCPA 1966).

Appellants respectfully request that the Examiner's rejections be withdrawn with direction to allow all of the claims pending in this application and pass this case to issue.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



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